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8-5-91
#4/Priority
Paper

CERTIFICATE OF MAILING

I hereby certify that this paper and every paper referred to therein as being enclosed is being deposited with the U.S. Postal Service as first class mail, postage prepaid, in an envelope addressed to: Commissioner of Patents & Trademarks, Washington, DC 20231,

on MARCH 13, 1991 (Date of Deposit)

3/13/91 Dana Grunsky
Date Name

File No: 2954/06403

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

MICHAEL BIRSHA DAVIES, DAVID JOHN HEARNE, PAUL KENNETH RAND
and RICHARD IAN WALKER

Serial No: 663,145

Group Art Unit:

Filed: 1 March 1991

Examiner:

For: INHALATION DEVICE

CLAIM FOR PRIORITY

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

Applicant hereby claims priority under 35 U.S.C.
Section 119 based on United Kingdom Patent Application No. 90
04781.2, filed 2 March 1990.

A certified copy of the priority document is submitted
herewith.

Respectfully submitted,

Dated: March 13, 1991

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Paul Fields
Reg. No. 20,298
Attorney for Applicant(s)

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I, the undersigned, being an officer duly authorised in accordance with Section 62(3) of the Patents and Designs Act 1907, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or the inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words, "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Witness my hand this
6th day of FEBRUARY 1991 .

W. Russell

COC 1

IX Check List (To be filled in by applicant or agent)

A The application contains the following number of sheet(s)

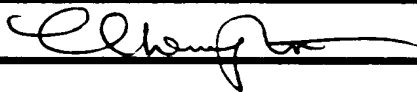
B The application as filed is accompanied by:-

1 Request 1 Sheet(s)
2 Description 18 Sheet(s)
3 Claim(s) - Sheet(s)
4 Drawing(s) 16 Sheet(s)
5 Abstract - Sheet(s)

1 Priority document -
Translation of priority document -
3 Request for Search -
4 Statement of Inventorship and Right to Grant -

X It is suggested that Figure No.....of the drawings (if any) should accompany the abstract when published.

XI Signature (See note 8)



NOTES:

1. This form, when completed, should be brought or sent to the Patent Office together with the prescribed fee and two copies of the description of the invention, and of any drawings.
2. Enter the name and address of each applicant. Names of individuals should be indicated in full and the surname or family name should be underlined. The names of all partners in a firm must be given in full. Bodies corporate should be designated by their corporate name and the country of incorporation and, where appropriate, the state of incorporation within that country should be entered where provided. Full corporate details, eg a "corporation organised and existing under the laws of the State of Delaware, United States of America", trading styles, eg "trading as xyz company", nationality, and former names, eg "formerly (known as) ABC Ltd" are not required and should not be given. Also enter applicant(s) ADP Code No.(if known).
3. Where the applicant or applicants is/are the sole inventor or the joint inventors, the declaration (a) to that effect at IV should be completed, and the alternative statement (b) deleted. If, however, this is not the case the declaration (a) should be struck out and a statement will then be required to be filed upon Patent Form No 7/77.
4. If the applicant has appointed an agent to act on his behalf, the agent's name and the address of his place of business should be indicated in the spaces available at V and VI. Also insert agent's ADP Code No. (if known) in the box provided.
5. An address for service in the United Kingdom to which all documents may be sent must be stated at VI. It is recommended that a telephone number be provided if an agent is not appointed.
6. The declaration of priority at VII should state the date of the previous filing and the country in which it was made and indicate the file number, if available.
7. When an application is made by virtue of section 8(3), 12(6), 15(4) the appropriate section should be identified at VIII and the number of the earlier application or any patent granted thereon identified.
8. Attention is directed to rules 90 and 106 of the Patent Rules 1982.
9. Attention of applicants is drawn to the desirability of avoiding publication of inventions relating to any article, material or device intended or adapted for use in war (Official Secrets Acts, 1911 and 1920). In addition after an application for a patent has been filed at the Patent Office the comptroller will consider whether publication or communication of the invention should be prohibited or restricted under section 22 of the Act and will inform the applicant if such prohibition is necessary.
10. Applicants resident in the United Kingdom are also reminded that, under the provisions of section 23 applications may not be filed abroad without written permission or unless an application has been filed not less than six weeks previously in the United Kingdom for a patent for the same invention and no direction prohibiting publication or communication has been given or any such direction has been received.

PATENTS ACT 1977

02 MAR 1990

PATENTS FORM NO. 1/77 (Revised 1982)

(Rules 16, 19)

The Comptroller
The Patent Office

9004781.2

REQUEST FOR GRANT OF A PATENT

THE GRANT OF A PATENT IS REQUESTED BY THE UNDERSIGNED ON THE BASIS OF THE PRESENT APPLICATION

I Applicant's or Agent's reference (*Please insert if available*) GAB/CJ ID091

II Title of invention
Device

III Applicant or Applicants (*See note 2*)

Name (First or only applicant).....GLAXO GROUP LIMITED.....

Country...UK.....State.....ADP Code No..00473587001 ✓ *NE*

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Name (of second applicant, if more than one).....

.....Country.....State.....

Address.....

IV Inventor (see note 3)

~~(a) The applicant is/are the~~
~~sole/joint inventor(s)~~ ~~xxx~~

or

(b) A statement on Patents Form
No 7/77 ~~is~~ will be furnished

V Name of Agent (if any) (*See note 4*)

ELKINGTON AND FIFE

ADP CODE NO
67034 ✓

VI Address for Service (*See note 5*)

Beacon House
113 Kingsway
London WC2B 6PP

VII Declaration of Priority (*See note 6*)

Country

Filing date

File number

VIII The Application claims an earlier date under Section 8(3), 12(6), 15(4), or 37(4) (*See note 7*)

Earlier application or patent number.....and filing date.....

DEVICE

This invention relates to an inhalation device by means of which a user can inhale medicament in the form of a powder.

Inhalation devices are known for use with blister packs in which the medicament is held in powder form in the blisters thereof. Such devices include a puncturing member which punctures each blister in turn, thus enabling the medicament to be inhaled therefrom. It is an object of the present invention to provide an inhalation the design of which has the potential, if desired, to handle a medicament pack having a large number of unit doses, without the device becoming unacceptably large.

According to the present invention there is provided an inhalation device for use with a medicament pack in which at least one medicament container is defined between two sheets peelably secured to one another, the device comprising means defining an opening station for the said at least one container; means for peeling the sheets apart at the opening station to open the container; and an outlet, communicating with the opened container, through which a user can inhale medicament from the opened container.

Preferably the medicament pack is formed from two

elongate sheets which define a plurality of medicament containers spaced along the length thereof, means being provided for indexing each container in turn to the opening station.

The invention also provides a medicament pack which may be used, for example, in the above device, the pack comprising an elongate strip having along its length a plurality of openable containers each containing an inhalable powdered medicament, the strip being sufficiently flexible to be wound into a roll. The invention further provides an inhalation device which is capable of receiving such a pack and dispensing powdered medicament to a patient.

In the accompanying drawings:

Figure 1 is a front view of a first embodiment of the invention;

Figure 2 is a rear view of the embodiment of Figure 1;

Figure 3 is an axonometric exploded view of the components of the embodiment of Figures 1 and 2;

Figures 3a, 3b and 3c are an axonometric view, a longitudinal section and an end view (partly broken away) showing a clutch used in the embodiment of Figures 1 to 3;

Figures 4a and 4b are an axial section and cross-section respectively, on a larger scale than Figures 1 to 3, of a mouthpiece which may be used in the first

embodiment (or in some other embodiment);

Figure 5 is a front view of a second embodiment, with a cover thereof removed to show the interior;

Figure 6 is a left side view of the second embodiment;

Figure 7 is a right side view of the second embodiment;

Figure 8 is a rear view of the second embodiment;

Figure 9 is also a rear view of the second embodiment, but showing the interior thereof;

Figure 10 is a top view of the second embodiment;

Figure 11 is an axonometric front view of the second embodiment;

Figure 12 is an axonometric rear view of the second embodiment;

Figure 13 is an axonometric exploded view of the second embodiment;

Figure 14 is a perspective view of a third embodiment;

Figure 15 is a front view of the third embodiment, showing the interior structure thereof;

Figure 16 is an axial view, on a larger scale, showing the mouthpiece of the third embodiment;

Figure 17 is a view from below of the third embodiment;

Figures 18 to 22 show a modified clutch which may be used in the invention, and are, respectively, a

front view, a top view, a back view, a left side view and an axonometric view; and--

Figures 23 to 25 show successive positions of operation of another embodiment of the invention, in rear view.

Referring now to Figures 1 to 3, these show an inhalation device in which is mounted a flexible strip 1 defining a plurality of pockets 2 each of which contains a dose of medicament which can be inhaled, in the form of a powder. The strip 1 comprises a base sheet 3 in which blisters are formed to define the pockets 2, and a lid sheet 4 which is sealed to the base sheet 3 except in the region of the blisters, in such a manner that the lid sheet and the base sheet can be peeled apart. The lid and base sheets are each preferably formed of a plastics/aluminium laminate, and the lid and base sheets are preferably adhered to one another by heat sealing. By way of example, the lid material may be a laminate consisting of 50 gsm bleach kraftpaper/12 micron polyester (PETP) film/20 micron soft temper aluminium foil/9 gsm vinylic peelable heat seal lacquer (sealable to PVC), and the base material may be a laminate 100 micron PVC/45 micron soft temper aluminium foil/25 micron orientated polyamide. The lacquer of the lid material is sealed to the PVC layer of the base material to provide the peelable seal between the lid and base sheets.

The strip 1 is shown as having elongate pockets which run transversely with respect to the length of the strip. This is convenient in that it enables a large number of pockets to be provided in a given strip length. The strip may, for example, be provided with sixty or one hundred pockets, but it will be understood that the strip may have any suitable number of pockets.

The inhalation device comprises a body 10 defining three storage chambers, namely a chamber 11 in which the strip 1 is initially housed and from which it is dispensed, a chamber 12 for receiving the used portion of the base sheet 3, and a chamber 13 within which the used portion of the lid sheet can be wound up on a wheel 14. The chambers 11 and 12 contain respective curved leaf springs 28 and 29, the purpose of which is described below. The body defines a further chamber 15 which houses an index wheel 16. This has a plurality of grooves 17 extending parallel to the axis of the wheel 16. The grooves are spaced at a pitch which is equal to the distance between the centre lines of adjacent pockets 2. The chambers 11, 12, 13 and 15 are closed by a lid 30. The chamber 15 communicates with the chambers 11, 12 and 13 via passages 31, 33 and 32 respectively.

The chamber 15 communicates via a slit 18 which, in turn extends upwardly within a mouthpiece 20. The slot 18 also communicates with air inlets, as will be

described below with reference to the specific mouthpiece shown in Figures 4a and 4b. The mouthpiece 20 is provided with additional air inlets 21 shown here in the form of a pair of circular apertures, though they may be of some other shape, as they are in Figures 4a and 4b. The primary purpose of the additional air inlets 21 is to provide additional air to the user and thus reduce the resistance to inhalation, though they may serve one or more additional purposes, as they do in Figure 4a and 4b and as is described below with reference to those Figures.

Means are provided by which the user can rotate the index wheel and the lid wheel in steps of a predetermined size. This means comprises a ratchet wheel 22 and a gear wheel 23, both connected to rotate in unison with the index wheel 16, a lever 24 arranged to rotate about the same axis as the ratchet wheel 22 and gear wheel 23, but independently thereof, and a gear wheel 25 which meshes with the gear wheel 23 and is arranged to rotate the lid wheel 14. The lever 24 carries a pusher arm 26, the end of which is arranged to engage the teeth of the ratchet wheel 22. The teeth of the ratchet wheel are also engaged by a pawl 27 fixedly secured to the body 10. For reasons which will become apparent from the description below of the operation of this embodiment, the gear wheel 25 is not connected directly to the lid wheel 14, but is

connected via a slipping clutch 50 which is housed within the lid wheel 14. The effect of the provision of this clutch is that slipping occurs between the lid wheel and the gear wheel 25 when the force required to rotate the lid wheel exceeds a predetermined amount.

The clutch 50 comprises a disc 51 provided with radially extending serrations 52, or other surface roughness, which is held in engagement with a similarly serrated or roughened surface 53 provided on an end face of the lid wheel 14 by a compression spring 54. The spring 54 bears at one end against an inwardly directed surface 55 of the lid wheel and at the other end against a nut 56 threaded on a bolt 57.

The device described above can be made so as to be reusable after the doses of medicament contained in the pockets 2 have all been dispensed. In that case, provision can be made for the user to gain access to the interior of the device, for example by removing the lid 30, so as to insert therein a fresh strip 1, for example in a cassette. Alternatively, however, the device may be made to be disposable once the strip 1 with which it is supplied has been used up.

In either event, when the device is first used the bulk of the strip 1 is within the chamber 11, kept in a relatively tight reel by the leaf spring 28, with a short portion at the leading end thereof passing out of the chamber 11 through the passage 31 to the index

wheel 16. The foremost part of the leading end of the strip is peeled apart so that the leading end of the lid sheet 4 can be secured to the lid wheel 14, and so that the leading end of the base sheet 3 can enter the passage 33. The end of the lid sheet 4 is held in place on the lid wheel 14 by means of a key 34 which is a force fit in a slot 35 in the wheel 14.

A user desiring to use the device pushes the lever 24 in an anticlockwise direction, so that the pusher arm 26 urges the ratchet wheel 22 through an angle equal to the angular distance between two adjacent teeth. This causes the ratchet wheel 16 to rotate by an angular amount equal to the pitch of the groove 17 thereof and thus equal to the distance between two adjacent pockets 2 in the strip 1. This brings a pocket 2 opposite the slot 18 in the body 10. Since the ratchet wheel 22 and gear wheel 23 move in unison, and since the gear wheel 25 meshes with the gear wheel 23, movement of the lever 24 also causes the lid wheel 14 to rotate. This peels a sufficient portion of the lid sheet 4 away from the base sheet 3 to expose the contents of the pocket 2 which is being brought into alignment with the slot 18.

When the user inhales through the mouthpiece 20 the flow of air which this produces entrains powder from the opened pocket, so that the powder is inhaled by the user. One way in which this can occur is

explained in more detail below with reference to the embodiment of mouthpiece shown in Figures 4a and 4b. Each time the above procedure is repeated a further length of lid sheet is wrapped around the lid wheel 14 and a further length of base sheet enters chamber 12 through passage 33. The leaf spring 29 therein ensures that the base sheet is coiled up and does not snag on the wall of the chamber 12.

One effect of winding up the lid sheet on the lid wheel 14 is that the external diameter of the wheel plus the sheet wound thereon gradually increases. Were it not for the use of a slipping clutch to connect the gear wheel 25 to the lid wheel 14 this would have the result that successive operations of the lever 24 would try to cause a progressively longer length of lid sheet to be wound on to the lid wheel. The slipping clutch 50, however, avoids this effect, the clutch slipping each time by an amount sufficient to ensure that for every operation of the lever the amount of lid sheet wound on is precisely equal to the pitch of the pockets 2.

Figures 4a and 4b show a portion of the index wheel 16 with a pocket 2 therein, in conjunction with a mouthpiece which differs slightly from the mouthpiece 20 shown in Figures 1 to 3, and which is denoted by reference numeral 120. The mouthpiece 120 has air inlets 140, to which reference in general terms has

already been made in connection with Figures 1 to 3, and a central powder outlet 119, one end of which is open to the pocket 2 and the other end of which opens into the interior of the mouthpiece 120.

When a user inhales through the mouthpiece 120 this causes air to flow in through the inlets 140 and thence through the pocket 2, into the powder outlet 119, and out through the mouthpiece 120. By thus directing the flow of air through the pocket 2, efficient entrainment of powder in the airflow is achieved, with consequent efficient emptying of the pocket. The mouthpiece 120 is provided with additional air inlets 121, shown here by way of example as being four in number, which open tangentially into the mouthpiece. When the user inhales air is drawn into the mouthpiece not only through the air inlets 140 but also through the air inlets 121, and the air entering through the inlets 121 produces a swirling airflow which helps to distribute powder effectively within the airflow and reduce the extent to which powder is deposited on the inside of the mouthpiece.

An alternative clutch arrangement is shown in Figures 18 to 22. In this, the index wheel 16 and the lid wheel 14 have respective toothed gear wheels 63 and 64 secured to them for rotation therewith. The direction of rotation is indicated by arrows in Figure 20.

Gear wheel 63 has a toothed surface 65, with the teeth being provided continuously all the way round the surface 65 and at a constant pitch. By contrast, the gear wheel 64 has a toothed surface 66 from which some teeth are missing by virtue of the provision of radially extending slots 67. The circumferential width of each slot at the surface 66 is equal to one tooth pitch. The drawings show three such slots, but it should be understood that there could instead be one slot, two slots, or more than three slots. To one side of each of the slots 67, in fact upstream of each slot as considered in the direction of rotation of the gear wheel 64, a toothed section 68 is defined between the slot 67, and a narrow slit 69. The radially inner end of each slit 69 communicates with an aperture 70, so that each toothed portion 68 is connected to the remainder of the gear wheel 64 only by an arm 71. The gear wheel 64, or at least those portions thereof which provide the arms 71, is made of a material which permits the toothed portions 68 to flex resiliently back and forth in a circumferential direction. The rest position of the portions 68 is as shown in the drawings, but when a force is applied to a portion 68 in the direction of rotation of the gear wheel 64, the portion 68 can move so as to close the gap 67 at the radially outer end. This has the effect that a tooth is then "missing" not at the end of the slot 67 but at

the end of the slit 69.

When the circumferential force applied by the gear wheel 63 to the gear wheel 64 is below a predetermined level the toothed portions 68 remain in their rest positions and the gear wheel 64 behaves just as if it had a continuous toothed surface like that of gear wheel 63. However, if the load exceeds a predetermined value, each time a toothed section 68 meshes with the gear wheel 63 it is moved circumferentially to close up the slot 67 at its outer end and open the slit 69. This movement of the toothed section 68 by a distance equal to the tooth pitch has the effect of producing slippage of the gear wheel 64 with respect to the gear wheel 69 equal to one tooth pitch. In this way, the illustrated arrangement is able to permit a total slippage of the gear wheels with respect to one another by a maximum of a distance equal to three times the tooth pitch per revolution, and hence a corresponding slippage of the lid wheel and index wheel with respect to one another. As will be appreciated, providing more or fewer toothed sections than the three illustrated will permit more or less than this maximum slippage.

A second embodiment of the inhalation device according to the invention is shown in Figures 5 to 13. This is intended for use with a strip 201, similar to the strip 1 used in the first embodiment except as

regards the spacing of the pockets (for which see below). In many respect the second embodiment resembles the first embodiment, and components in the second embodiment which correspond in general terms to particular components in the first embodiment are denoted by the same reference numerals, but with the addition of 200. The main difference between the first embodiment and the second embodiment is that in the latter there is no index wheel corresponding to the index wheel 16 of the first embodiment. Instead, indexing of the strip 1, to ensure that each operation of the lever advances the strip by an amount equal to the pitch of the pockets, is achieved by a resiliently flexible arm 250 terminating in a tooth 252 which engages between adjacent pockets. Each time the lever 224 is operated the arm 250 is resiliently depressed as a pocket slides past the tooth 252 thereof, and the tooth then springs back into engagement with the strip to the rear of the pocket which has just passed it.

It will be appreciated that, as in the case of the first embodiment, the diameter of the lid wheel 214 with the lid sheet thereon gradually increases during operation. Since a slipping clutch cannot be used in this embodiment the effect just described is compensated by having the spacing of the pockets 2 gradually increasing towards the rear end of the strip.

One other difference which will be noted between

the first and second embodiments, is that in the latter the chambers 211 and 212 form a single composite chamber, unlike the separate chambers 11 and 12 in the first embodiment. However, this need not be so, and the first embodiment could use a single composite chamber and the second embodiment could use separate chambers.

Figures 14 to 17 show a third embodiment. In many respects this resembles the second embodiment, and components in the third embodiment which correspond in general terms to components in the second embodiment are denoted by the same reference numerals but with the addition of 300.

One difference which will be observed between the second and third embodiments is that in place of the lid wheel 114 a pair of wheels 314a and 314b are employed, with the lid sheet being gripped in the nip between the wheels 314a and 314b. These wheels are knurled or otherwise roughened to improve the grip between the wheels and the lid sheet. The used lid sheet is not wound up but is fed into a chamber 313, so that no problem arises, as it does in the first two embodiments, with the lid wheel attempting to wind up progressively longer lengths of lid as operation of the device continues.

Figure 16 shows the mouthpiece to be of a somewhat different design to that shown in Figures 4a

and 4b. The mouthpiece is shown as having a single air inlet 340 in place of the pair of air inlets 140, and the powder outlet 219 of Figures 4a and 4b is replaced by a mouthpiece portion 319 of reduced width. It should be understood, however, that the device shown in Figures 14 to 17 could be modified so as to incorporate a mouthpiece more closely resembling Figures 4a and 4b.

Figures 14 and 15 show the device as being provided with a hinged cover 360, and such cover could be provided for either of the first two embodiments. Figure 17 shows the device as having a window 370 through which indicia on the strip can be viewed. By printing the strip with numbers or other indicia which correlate with the number of pockets from which powder has been dispensed, or alternatively is to be dispensed, the user is provided with an indication of how many doses have been used or, alternatively, how many doses remain. Another possibility is to use a dose counting device driven by one of the rotating components of the inhalation device.

It should be noted that similar indicia and means for viewing those indicia could be provided in all the embodiments.

Figures 23 to 25 show an embodiment of the invention incorporating, as a further feature, indicia which instruct the user as to the successive steps

which the user is to take to operate the device. Apart from the indica, the device is largely the same as the embodiment shown in Figures 1 to 3, and the same reference numerals are used for the corresponding components. However, there are some additional components, as will be apparent from the following description.

The device shown in Figures 23 to 25 has a cover 400 which is pivotally connected to the remainder of the device for pivotal movement about an axis 401. The gear wheels 23 and 25 and the associated components are covered by a rear wall 402. This extends over the whole of the rear of the device, but in the drawings all except a small portion thereof is shown broken away for ease of understanding. The lever 24 is provided with an arcuate extension 403, on an edge whereof is formed a cam 404. The extension 403 carries indicia in the form of instructions to the user, in this case the legends "OPEN COVER", "PRESS BUTTON", "INHALE". When the lever 24, and hence the extension 403, are in particular positions a respective one of these legends is visible through a window 405 in the rear wall 402. The distal end of the extension 403 constitutes a button 406. The end of the lever 24 remote from the extension 403 carries a tongue 407 pivotal therewith.

Figure 23 shows the device in its rest position. The legend "OPEN COVER" is visible through the window

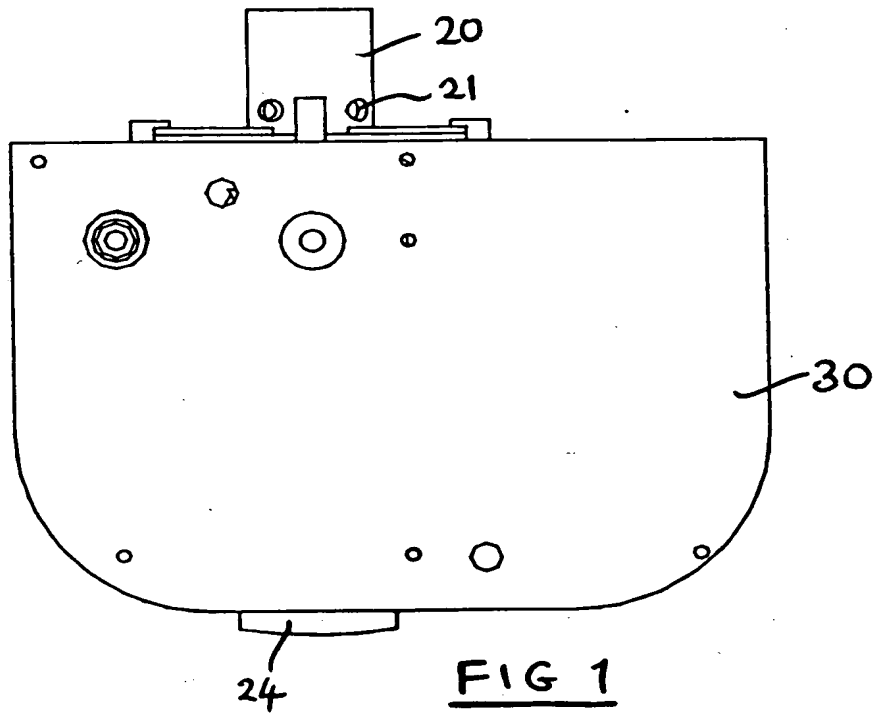
405. If a patient now opens the cover 400 this brings the device into the position shown in Figure 24. It will be seen that the top rear edge of the cover has struck the cam 404 and moved the extension 403 through an angle such as to make the legend "PRESS BUTTON" visible through the window 405. If the user now presses the button 406 this causes the lever 24 to rotate, thus opening a powder-containing container, as described in connection with Figures 1 to 3. This brings the device into the position shown in Figure 25, in which the legend "INHALE" is visible through the window 405. It will also be seen that in the position of Figure 25 the tongue 407 protrudes upwardly. Accordingly, when the user, having inhaled, closes the cover, the tongue 407 is struck by a lug 408 on the underside of the cover, which pushes the lever 24, with its extension 403, back into the position shown in Figure 23, once again causing the legend "OPEN COVER" to be displayed.

The device just described not only gives the step-by-step instructions to the user, thus reducing the risk of a patient being confused, but also makes it difficult for the patient to use the device other than in the intended manner, by virtue of the fact that the button 406, once depressed, is not again accessible until the user closed the cover and reopened it.

In the embodiments described above, reference is

made to a mouthpiece. However, if the device was to be used for purposes other than oral inhalation some other outlet would be employed, e.g. a nosepiece.

1/16



2/16

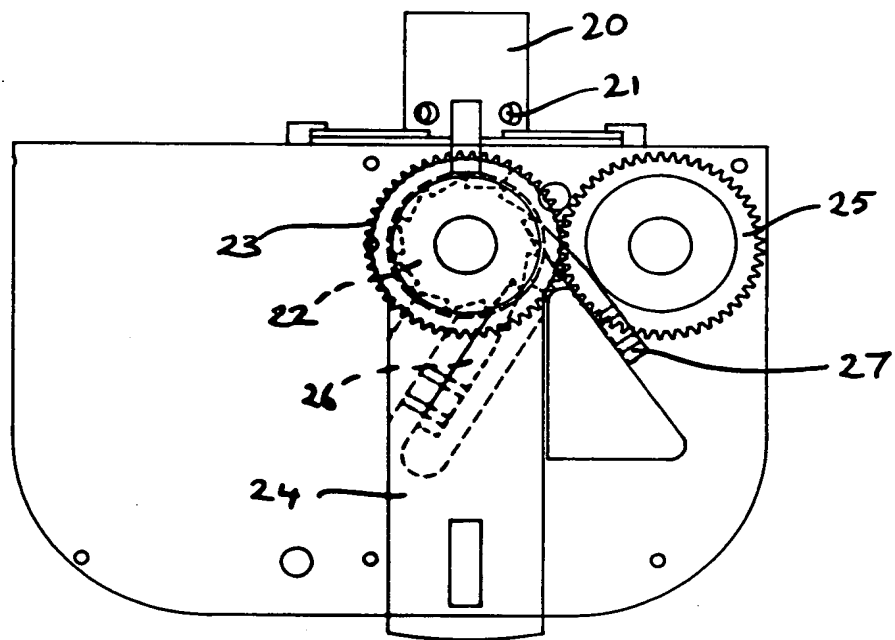


FIG 2

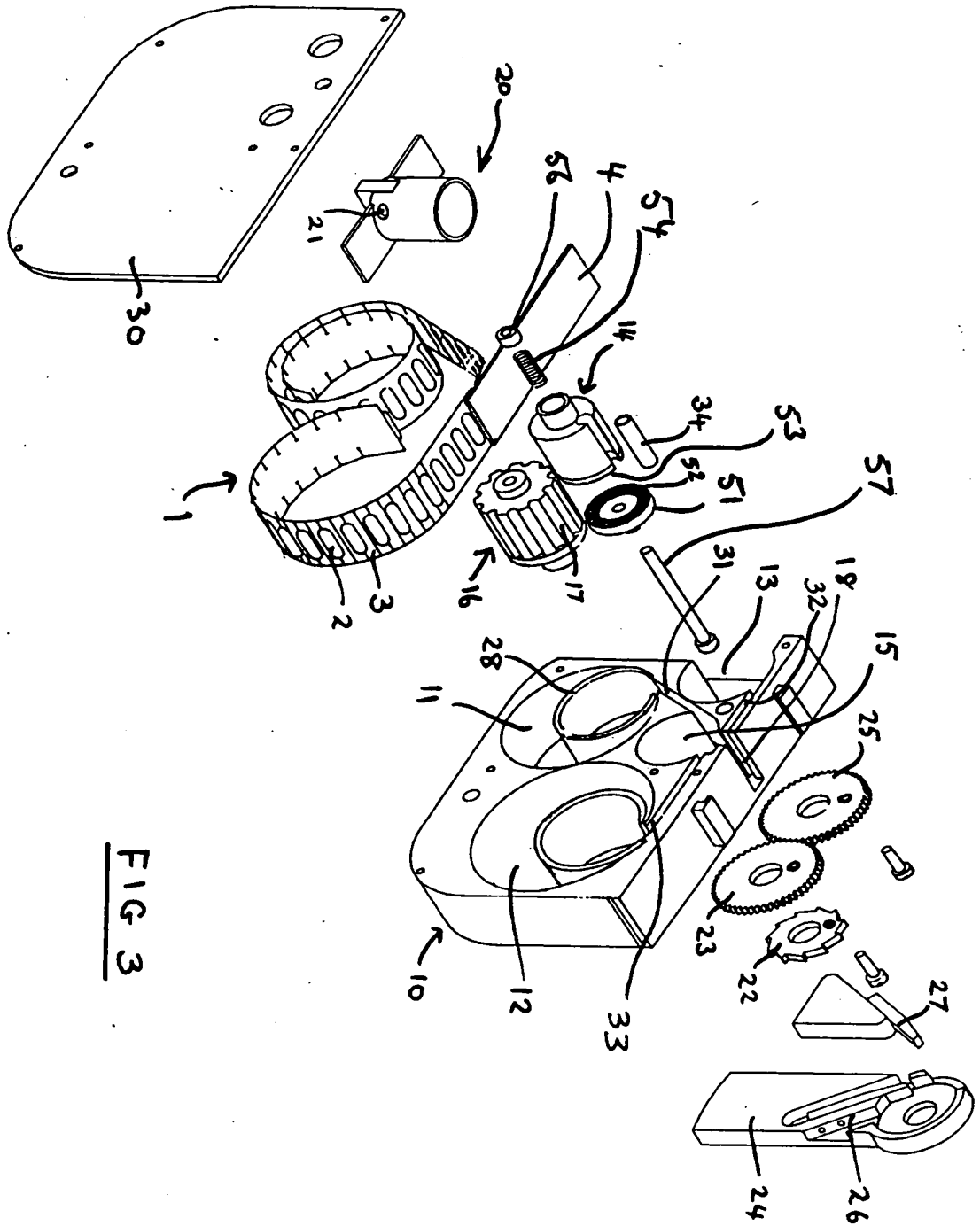
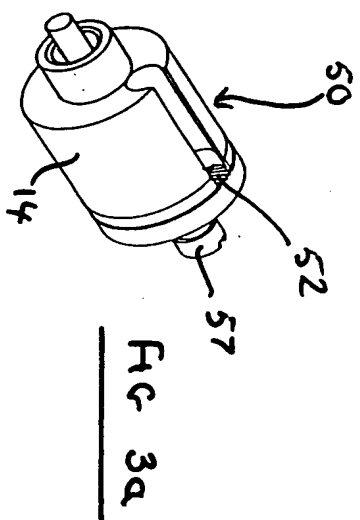
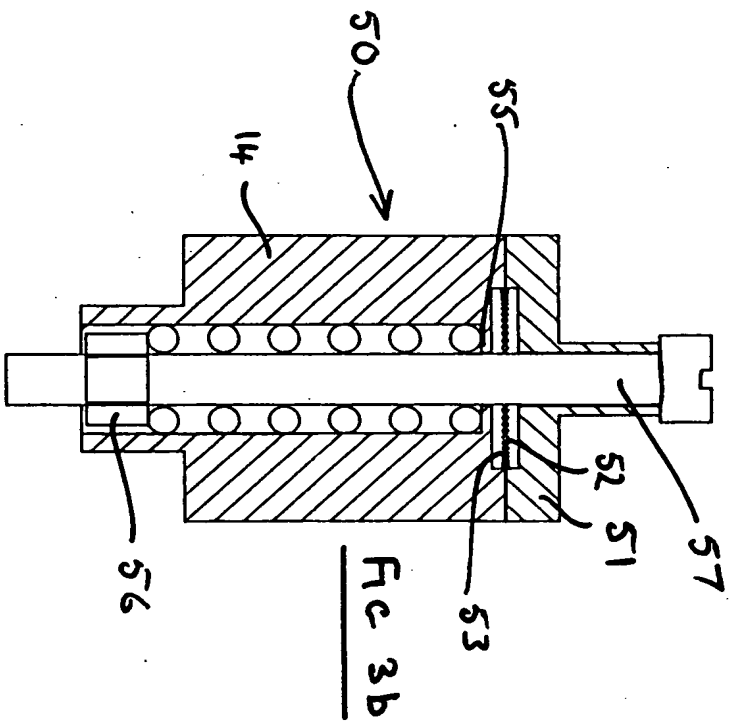
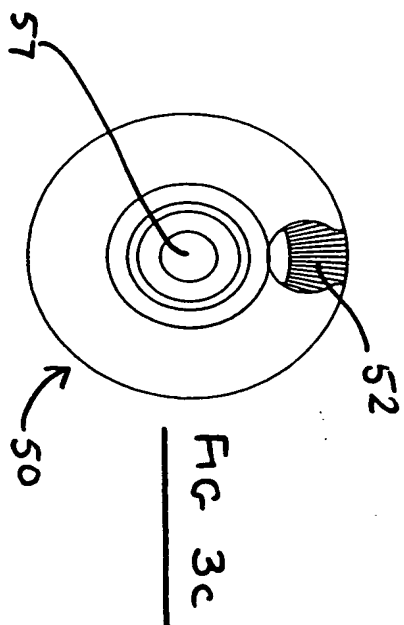


FIG 3



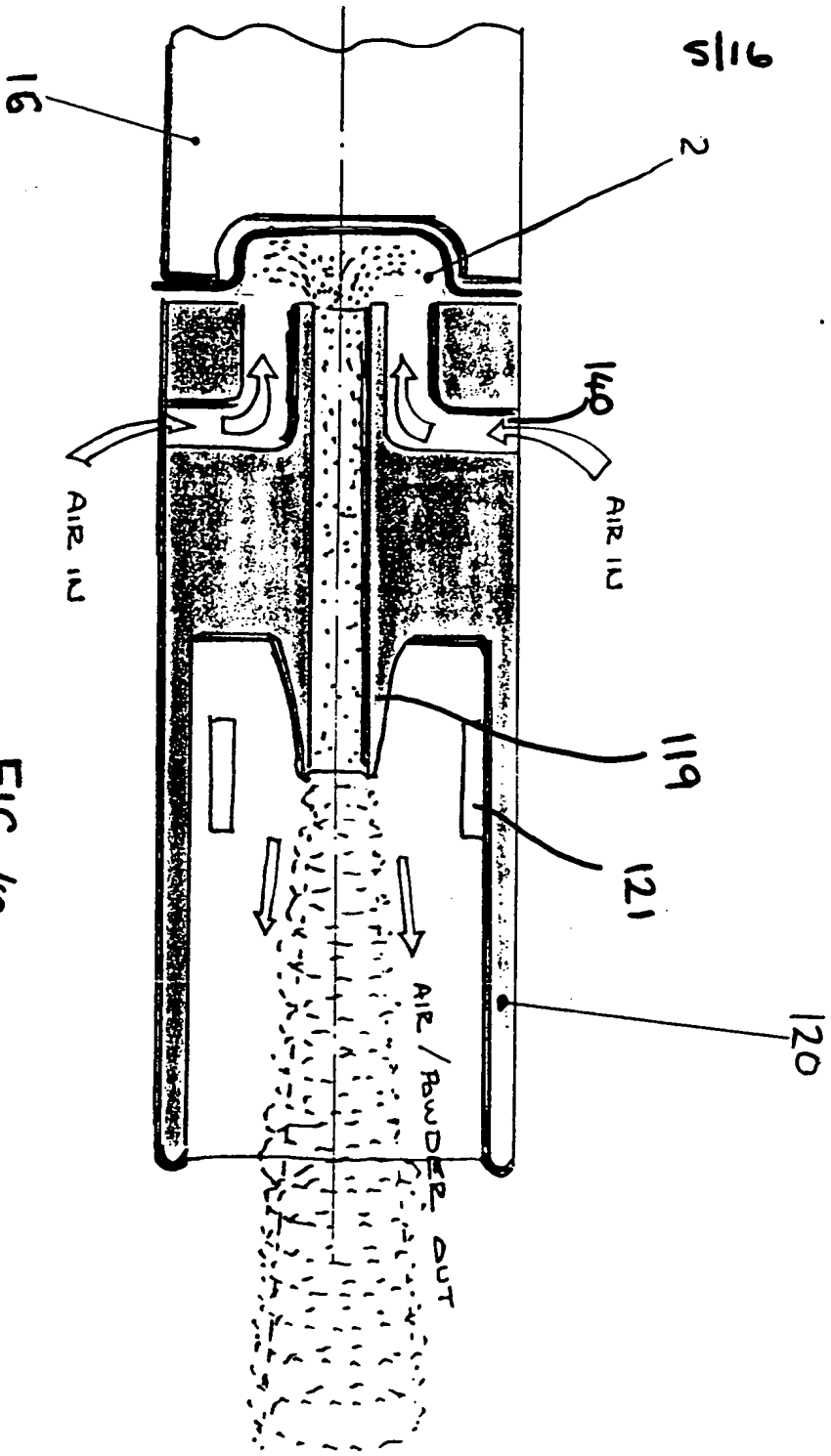


FIG 4a

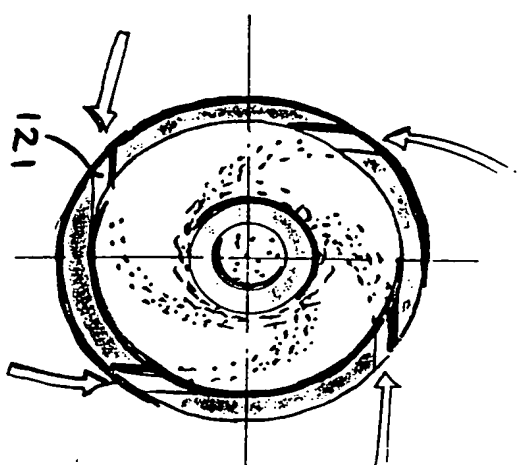


FIG 4b

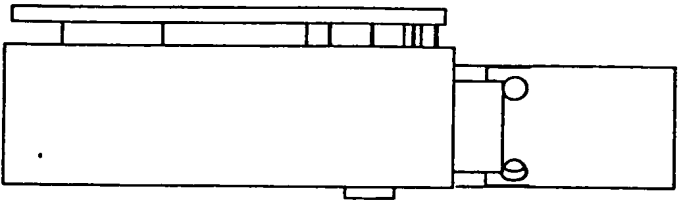


FIG 6

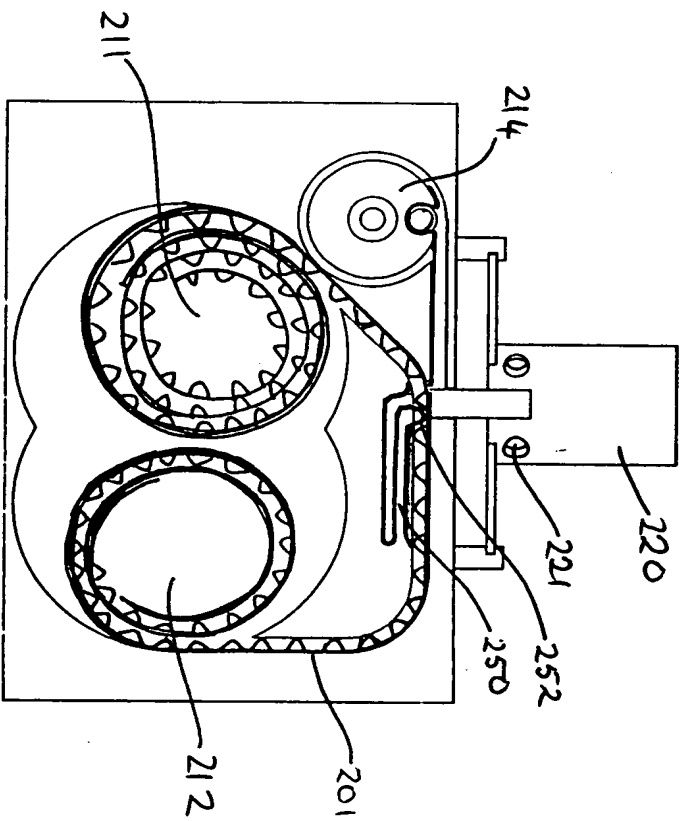


FIG 5

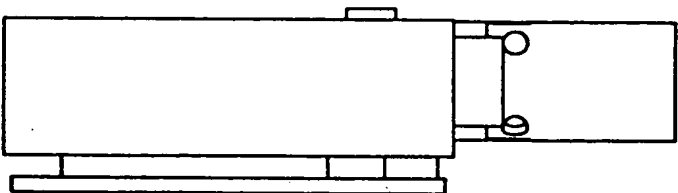


FIG 7

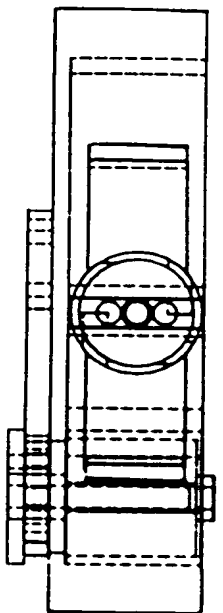


FIG 10

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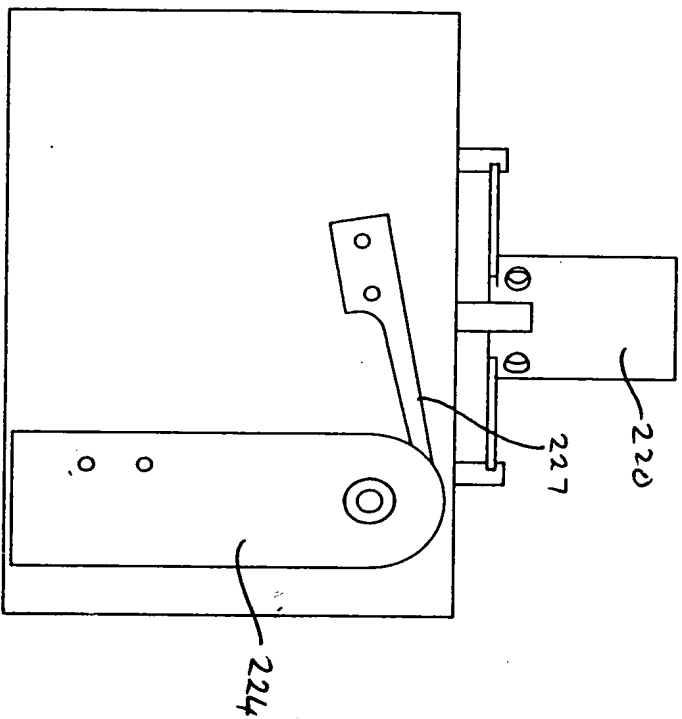


FIG 8

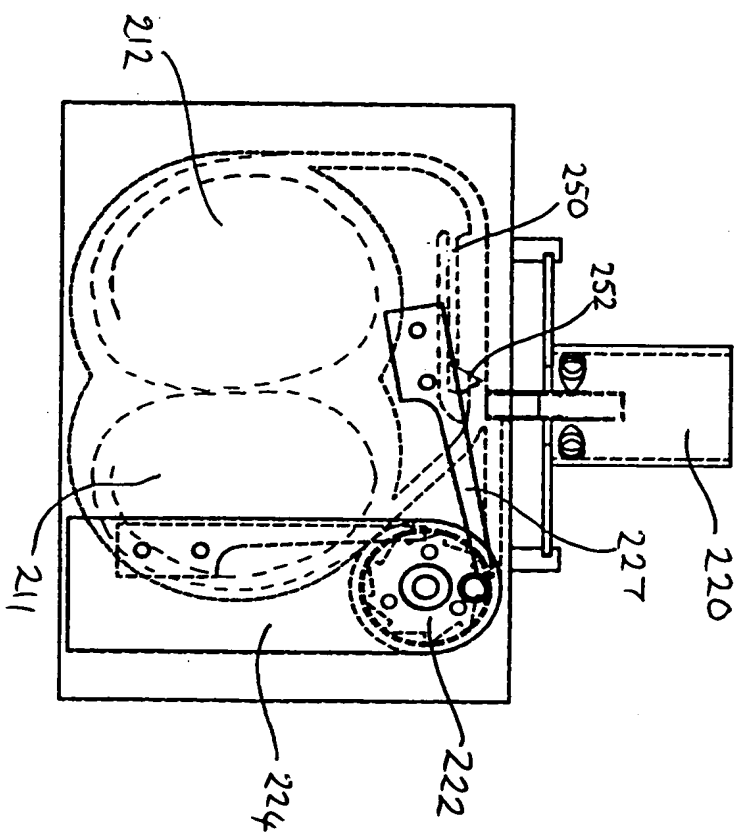


FIG 9

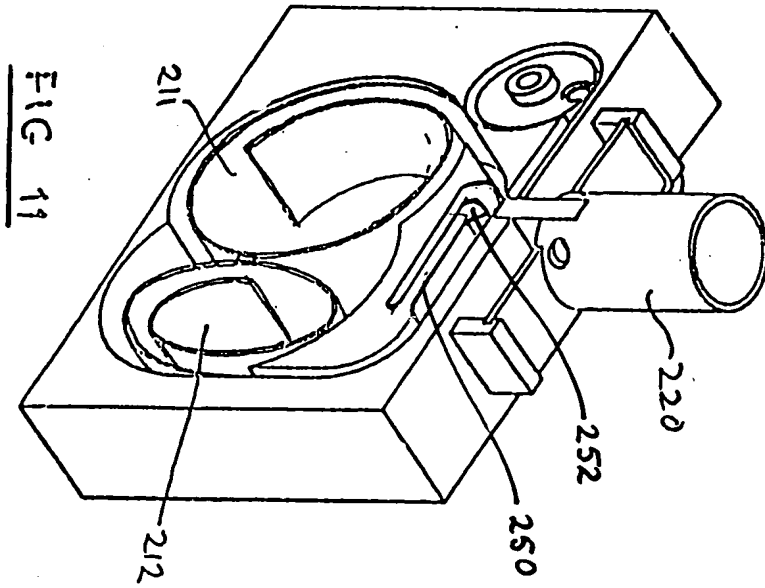


FIG 11

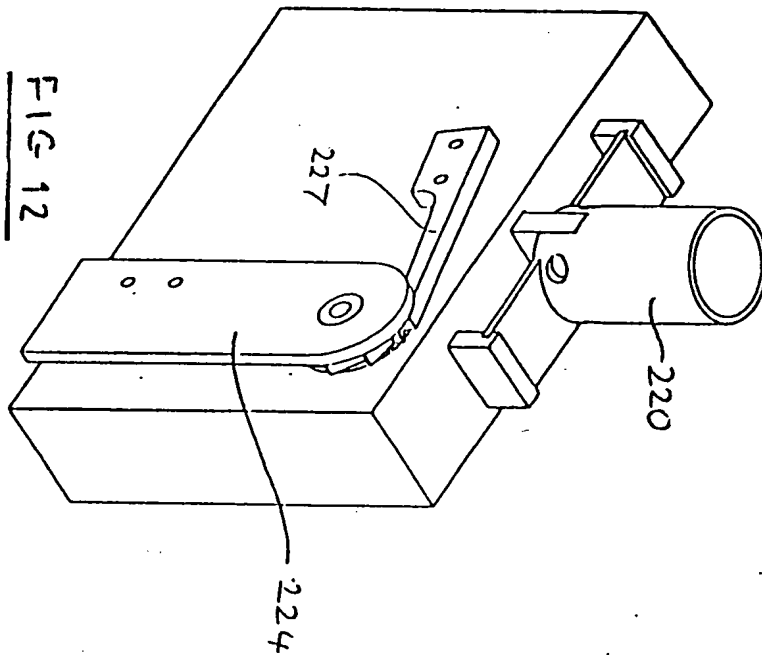
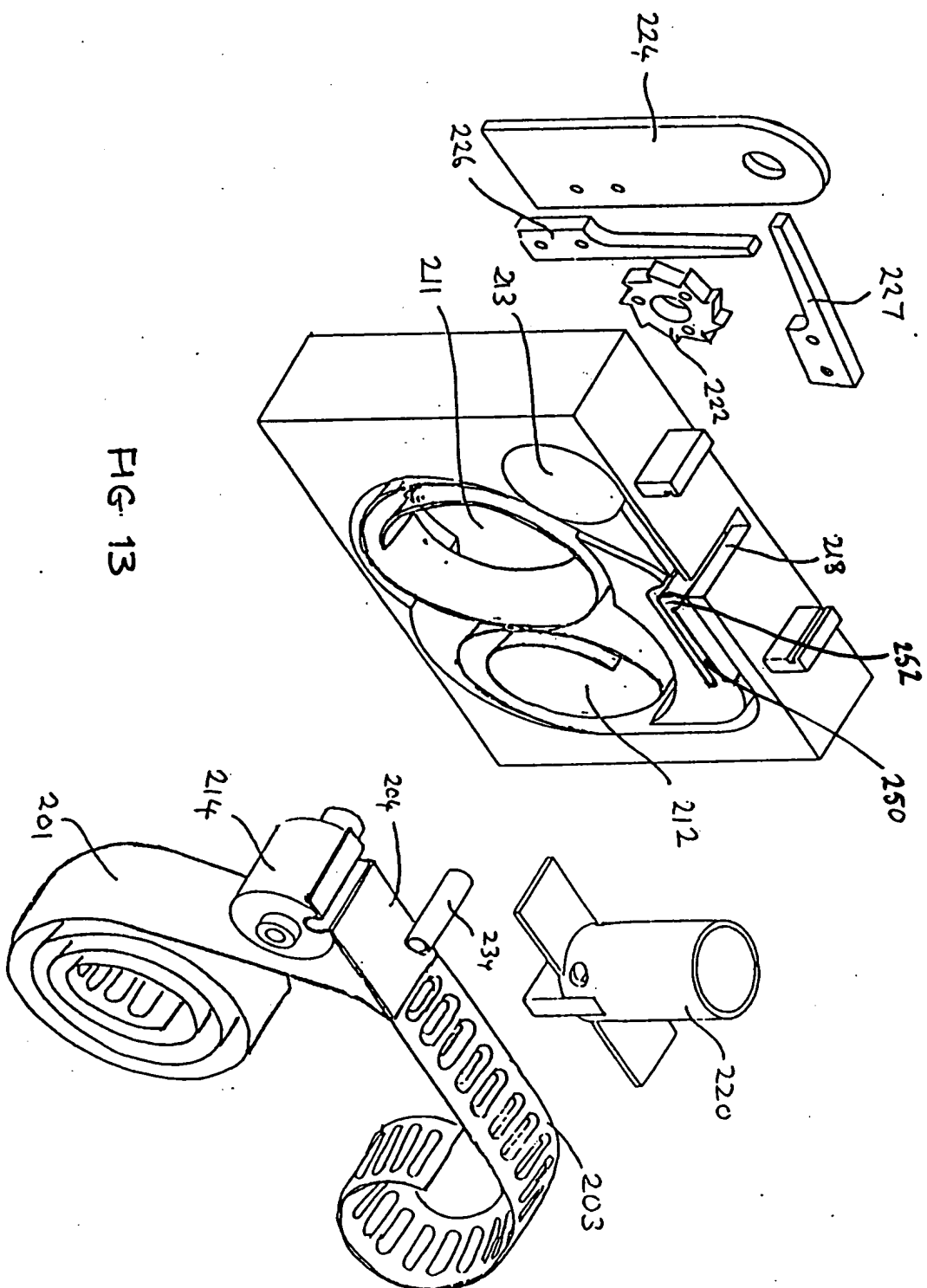


FIG 12



III

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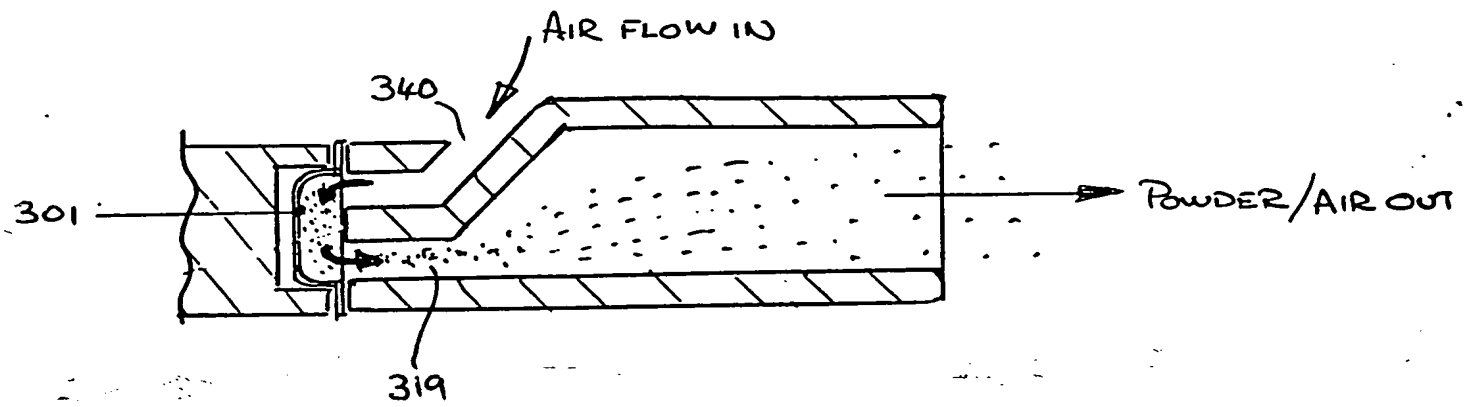


FIG 16

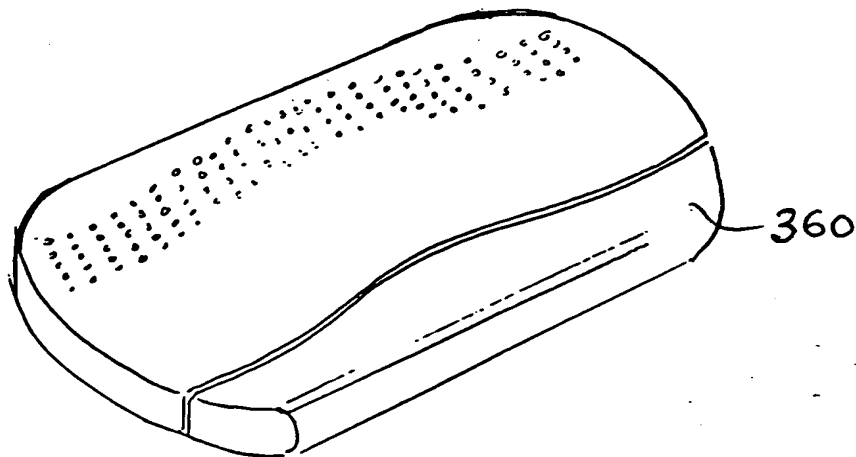


FIG 14

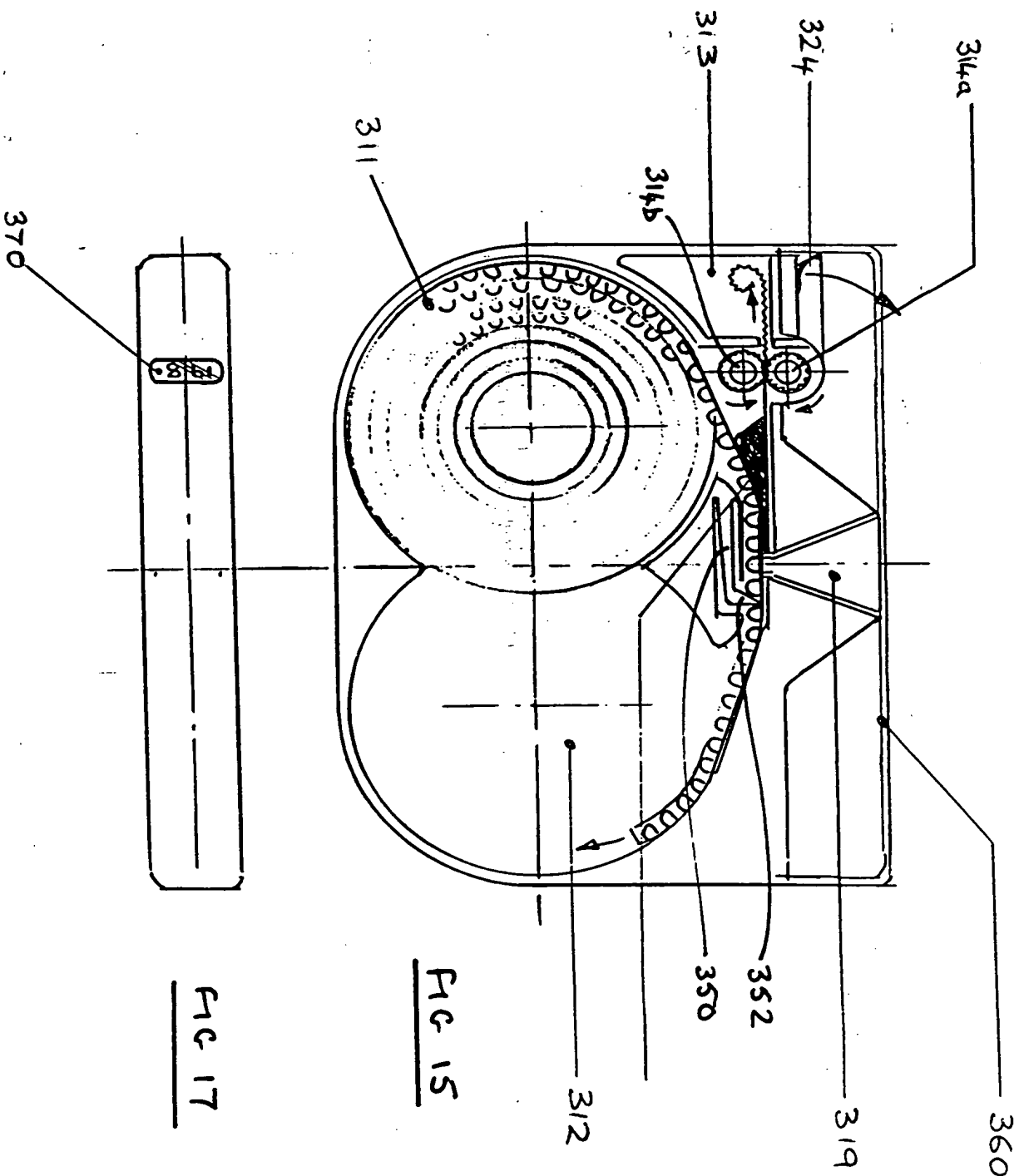


FIG 15

FIG 17

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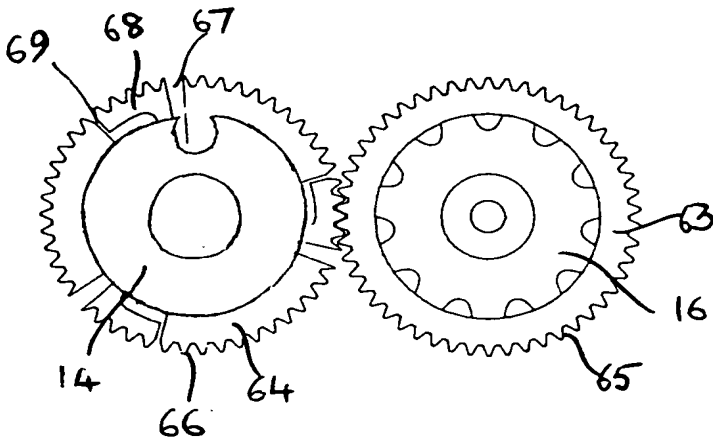


FIG 18

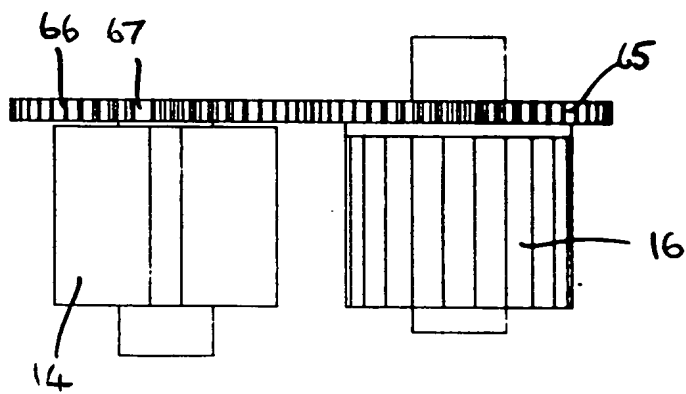


FIG 19

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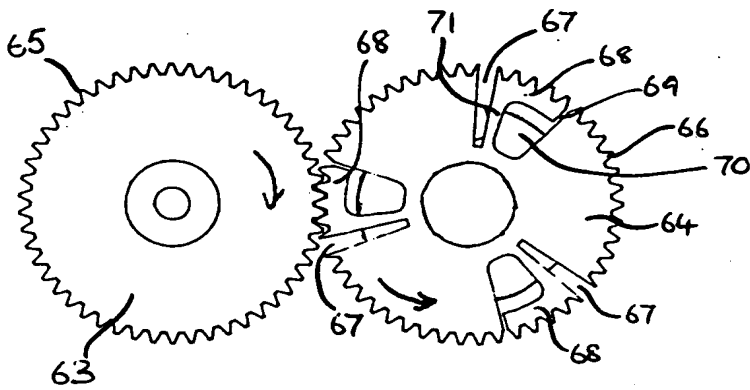


FIG 20

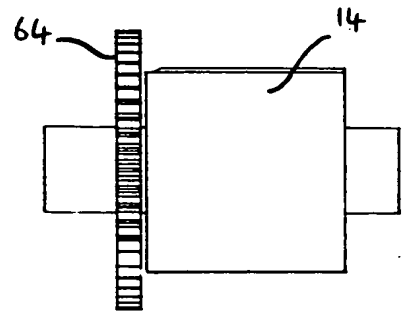


FIG 21

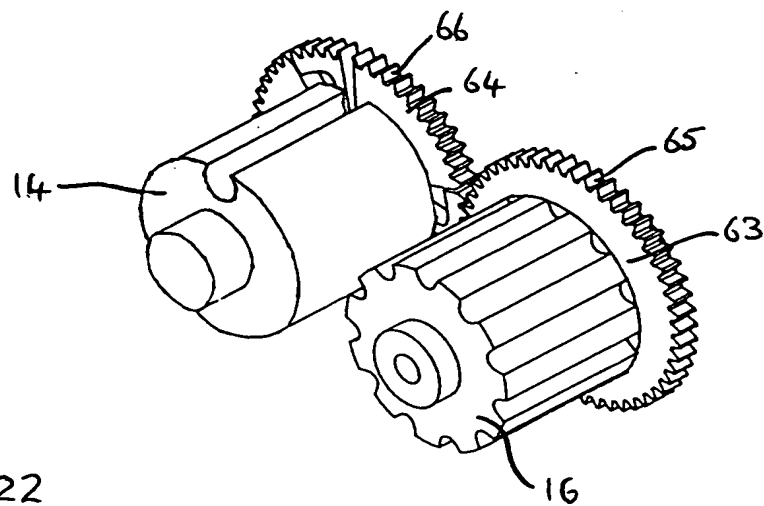


FIG 22

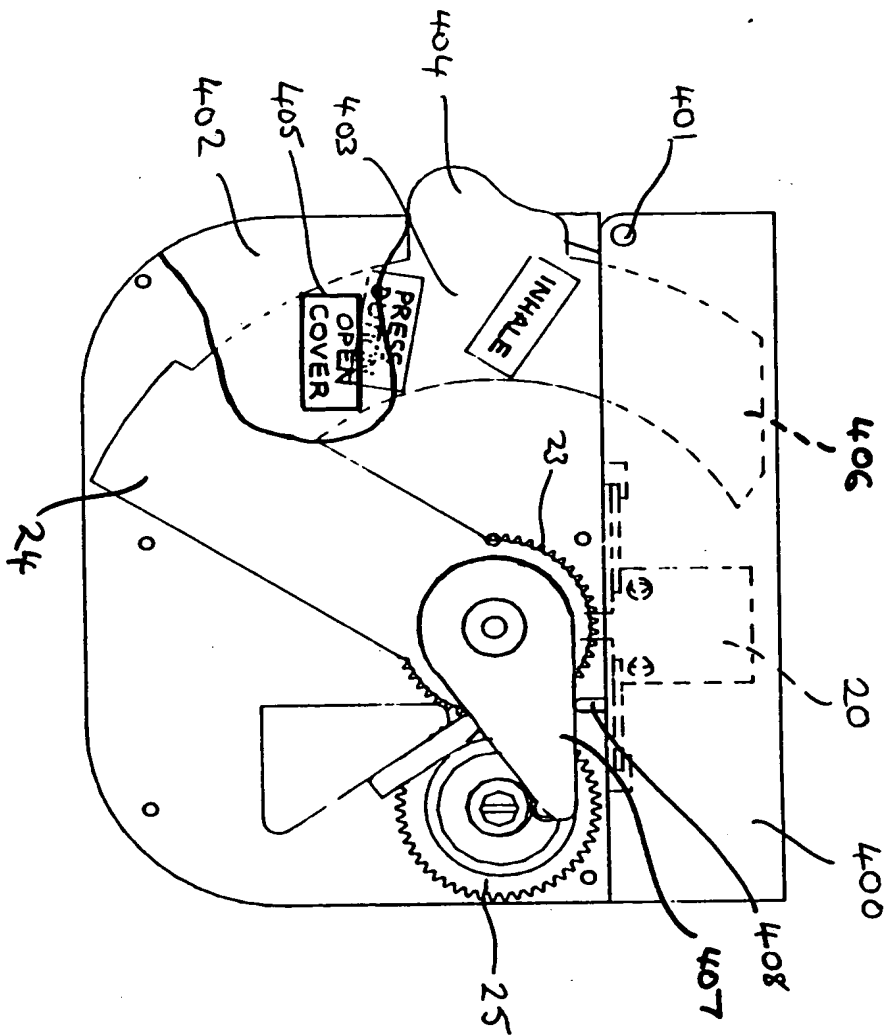


FIG 23

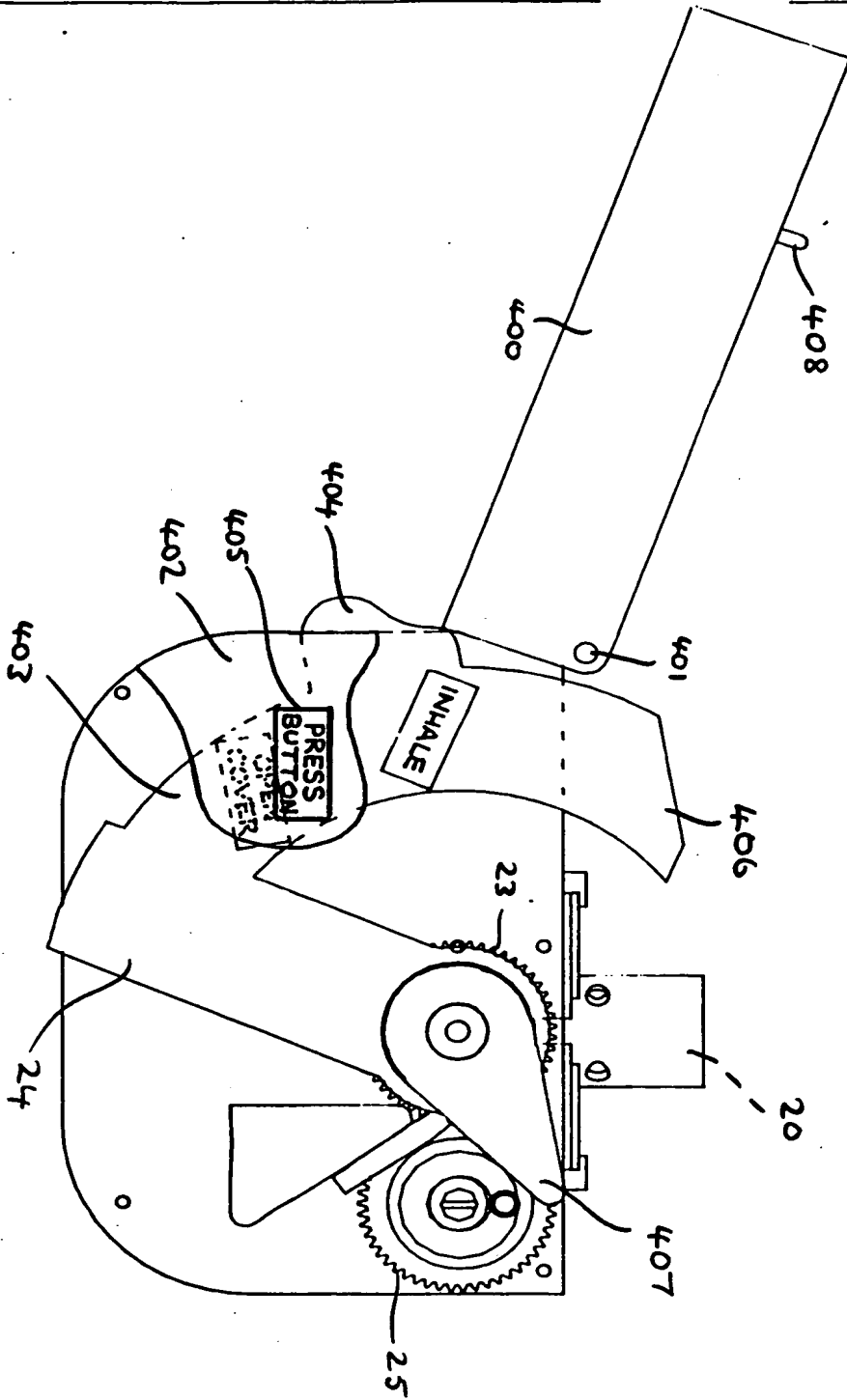


FIG. 24

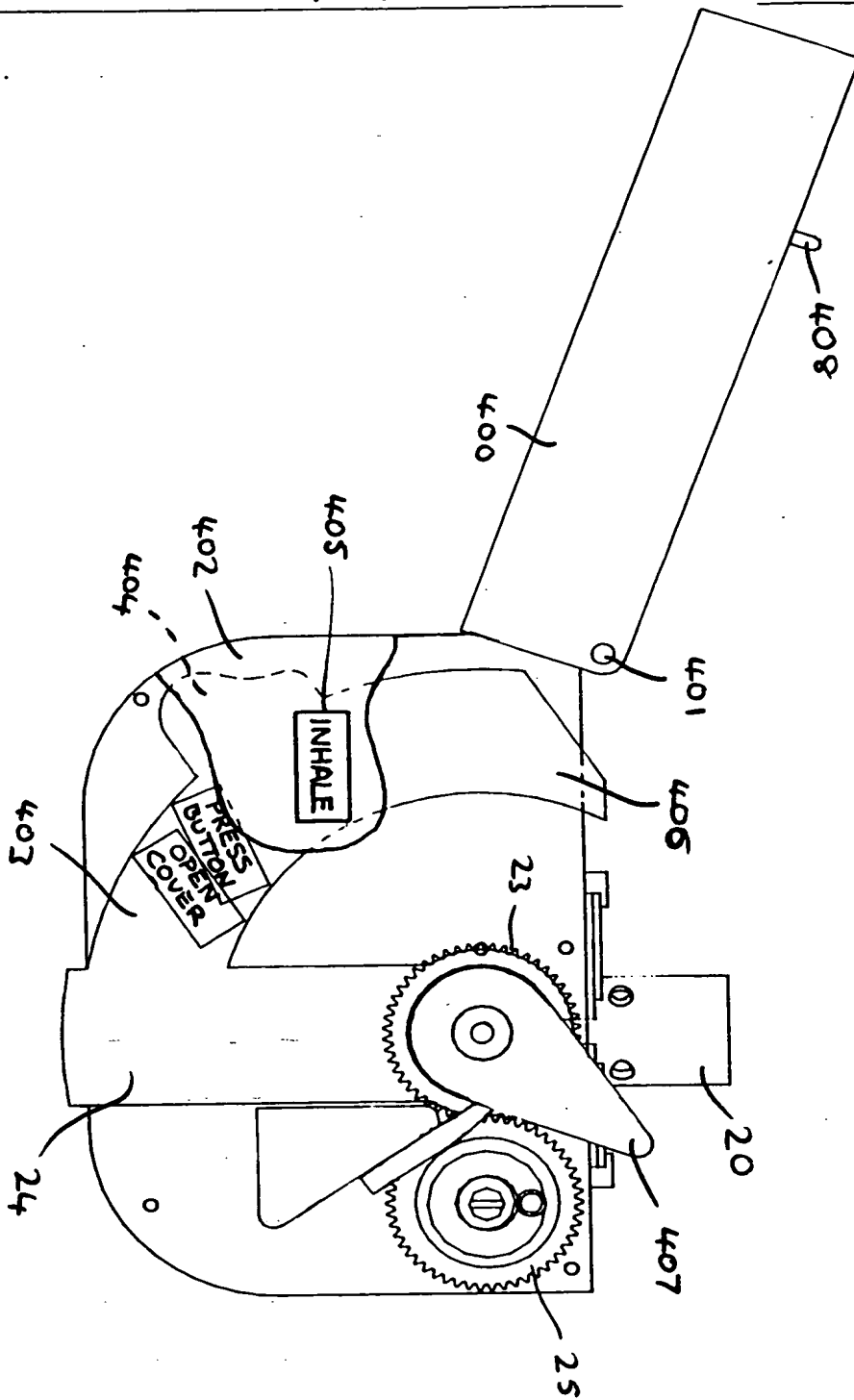


FIG 25